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ENHANCED EXPRESSION OF NEOPTERIN IN ACCUMULATED MACROPHAGES AT AORTIC VALVE STENOSIS IN PATIENTS WITH HEMODIALYSIS

ACC Oral Contributions
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Backgroud: There is an increased incidence of aortic valve stenosis (AS) in patients with hemodialysis (HD), and this could contribute to an excess cardiovascular mortality. However, little is known about the progression of AS in HD patients. Neopterin, a by-product of the guanosine triphosphate pathway, is produced by activated macrophages on stimulation by interferon-γ from T-lymphocytes and is capable of enhancing the oxidative potential of reactive oxygen species. In our recent study, enhanced expression of neopterin in macrophages was closely related to coronary and carotid plaque instability (Heart 93:1537-1541, 2007, Atherosclerosis 208:524-530, 2010). To elucidate the role of neopterin in the aortic valve of AS patients with HD, we immunohistochemically studied the presence of neopterin in aortic valve specimens from AS patients with and without HD.

Methods: Frozen aortic valve samples were surgically obtained from a cohort of 33 AS patients with HD (n=12) and non-HD (n=21). The samples were stained immunohistochemically with antibodies against smooth muscle cells, macrophages, T-lymphocytes, neutrophils, microvessels and neopterin. To identify the cell type that stained positive for neopterin, immunodouble staining was also performed.

Results: In 9 of the 12 patients (75%) with HD, abundant neopterin-positive cells were found in the aortic valve tissue samples. However, in 21 lesions from non-HD patients, only 6 lesions (29%) showed scatter neopterin-positive cells. Quantitatively, the percentage of the neopterin-positive area was significantly higher in patients with HD than in patients with non-HD ($P<0.0001$). Moreover, the percentage of the neopterin-positive area showed a significant positive correlation with the number of neutrophils and T-lymphocytes (neutrophils, $r = 0.67$, $P<0.0001$; T-lymphocytes, $r = 0.66$, $P<0.0001$). Double immunostaining for neopterin and macrophages demonstrated that the vast majority of the neopterin-positive cells were macrophages in HD patients.

Conclusions: These findings suggest that neopterin may be one of the mechanisms responsible for rapid progression of AS in HD patients.